Answer 1:

Bibliographic Information

Effect of methylprednisolone on growth of hepatocellular carcinoma in nude mice. Zeng, Jixiao; He, Xiaoshun; Ma, Yi; Zhu, Xiaofeng; Han, Ming; Zhang, Longjuan; Shi, Chengjun. Department of Organ Transplantation, The First Affiliated Hospital, Sun-Yat Sen University, Guangzhou, Peop. Rep. China. Zhonghua Shiyan Waike Zazhi (2007), 24(2), 190-192. Publisher: Hubei Sheng Yixuehui, Bianji Chubanbu, CODEN: ZSWZAA ISSN: 1001-9030. Journal written in Chinese. AN 2008:651001 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The effects of methylprednisolone on the hepatocellular carcinoma and the relevant mechanism were investigated. Twenty nude mice bearing s.c. xenograft human hepatocellular carcinoma (HCC) were randomly divided into 3 groups: the control group, low-dose group and high-dose group. The effect of methylprednisolone was evaluated after 4 wk, including the wt. of nude mice, the tumor vol. and wt. The blood concn. of α-fetoprotein (AFP) was measured by RIA. The expressions of vascular endothelial growth factor (VEGF) and matrix metalloproteinase-2 (MMP-2) were detected by fluorescent quant. polymerase chain reaction (FQ-PCR). Tumor wt. [(1.62±0.12) g vs. (1.33±0.19) g] and vol. [(0.63±0.05) cm3 vs. (0.56±0.05) cm3] were significantly increased in high-doe group as compared with the control group. The blood concn. of AFP was augmented in high-dose group [(7.50±1.14) μg/L vs. (5.98±0.78) μg/L]. The expressions of VEGF and MMP-2 were up-regulated significantly in high-dose group. The growth and metastasis in the nude mice were enhanced when exposed to high dose of methylprednisolone. The mechanism attributed to the up-regulation of VEGF and MMP-2 expressions probably.

Answer 2:

Bibliographic Information

Differential uptake of 18F-fluorodeoxyglucose by experimental tumors xenografted into immunocompetent and immunodeficient mice and the effect of immunomodification. Mamede, Marcelo; Saga, Tsuneo; Ishimori, Takayoshi; Nakamoto, Yuji; Sato, Noriko; Higashi, Tatsuya; Mukai, Takahiro; Kobayashi, Hisataka; Konishi, Junji. Department of Nuclear Medicine and Diagnostic Imaging, Graduate School of Medicine, Kyoto University, Shogoin, Sakyo-ku, Kyoto, Japan. Neoplasia (New York, NY, United States) (2003), 5(2), 179-183. Publisher: Nature Publishing Group, CODEN: NEOPFL ISSN: 1522-8002. Journal written in English. CAN 139:334896 AN 2003:328757 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

PURPOSE: To study the contribution of immunol. background to the uptake of fluorine-18-fluorodeoxyglucose (18F-FDG) by the tumor tissues. METHODS: The uptakes of 18F-FDG to the same exptl. tumor model (SCCVII) xenografted into immunocompetent and immunodeficient (athymic) mice were compared. In addn., the immunomodifying effect of steroid on the uptake of 18F-FDG by these tumors was investigated. RESULTS: The uptake of 18F-FDG by the tumors in immunocompetent mice was significantly higher than that in immunodeficient (athymic) mice. Although steroid pretreatment had no effect on the tumor uptake in immunodeficient mice, it significantly decreased the tumor uptake in immunocompetent mice. CONCLUSION: The higher tumor uptake of 18F-FDG obsd. in immunocompetent mice, modulated by steroid pretreatment, was contributed by the host immune reaction, probably cellular immunity employed by T-lymphocytes. These findings can clin. conclude that the intense accumulation of 18F-FDG in the metastatic lymph nodes, which contain only a small no. of cancer cells, was caused by the enhanced uptake of 18F-FDG by activated T-lymphocytes due to host immunity against cancer cells present in metastatic lymph nodes.

Answer 3:

Bibliographic Information

Decreased C-MYC and BCL2 expression correlates with methylprednisolone-mediated inhibition of Raji lymphoma growth.

Morris, Geoffrey; Denardo, Sally J.; Denardo, Gerald L.; Leshchinsky, Tatiana; Wu, Biao; Mack, Philip C.; Winthrop, Michelle D.; Gumerlock, Paul H. Section of Radiodiagnosis and Therapy and the Cancer and Molecular Research Laboratory, Division of Hematology/Oncology, Department of Internal Medicine, School of Medicine, University of California, Davis, Sacramento, CA, USA. Biochemical and Molecular Medicine (1997), 60(2), 108-115. Publisher: Academic, CODEN: BMMEF4 ISSN: 1077-3150. Journal written in English. CAN 127:29246 AN 1997:314158 CAPLUS

Abstract

Methylprednisolone (MP) and related corticosteroids are a fundamental part of regimens used to treat lymphoma and leukemia. In many of these malignancies, oncogenic activation of C-MYC and BCL2 is seen. Abnormalities of the tumor suppressor p53, which exerts growth-suppressing and apoptosis-enhancing functions through the transcriptional regulation of downstream genes including CDKN1, GADD45, and BCL2, are also often found. The goal was to det. the modulation of expression of the oncogenes (C-MYC and BCL2), the p53 pathway described above, and the apoptosis marker TGF-β1 in the human Raji lymphoma following MP treatment. Raji xenografts were grown in nude mice and growth curves characterized by sequential measurement. Mice were treated daily for 8 days with MP. Tumors were harvested untreated, or at 1 or 8 days after cessation of MP treatment, and the RNA was extd. RT-PCR was used to det. the level of mRNA expression of the genes. Tumor growth was greatly reduced in the MP-treated mice. Gene expression levels for C-MYC and BCL2 were reduced at 1 day following MP and approached control levels 8 days after MP treatment. Expression levels of p53, CDKN1, and GADD45 were moderately and coordinately decreased at 1 day after cessation of MP treatment and remained repressed a week later. TGF-β1 exhibited no change in expression levels. These results suggest that decreased expression of C-MYC and BCL2 may play a role in the mol. events that initiate and are responsible for the growth inhibition of Raji lymphoma xenografts by MP.

Answer 4:

Bibliographic Information

Methylprednisolone prevents rejection of intrastriatal grafts of xenogeneica embryonic neural tissue in adult rats. Duan, Wei-Ming; Brundin, Patrik; Grasbon-Frodl, Eva Maria; Widner, Hakan. Section for Neuronal Survival, Department of Physiology and Neuroscience, Biskopsgatan 5, Lund, Swed. Brain Research (1996), 712(2), 199-212. Publisher: Elsevier, CODEN: BRREAP ISSN: 0006-8993. Journal written in English. CAN 124:251210 AN 1996:200697 CAPLUS

Abstract

The effects of high-dose methylprednisolone on the survival of intrastriatal neural xenografts and the host responses against them. Dissocd. mesencephalic tissue from inbred mouse (CBA-strain) embryos was transplanted to the intact striatum of adult Sprague-Dawley rats. The rats received either daily injections of methylprednisolone (30 mg/kg), or cyclosporin A (10 mg/kg), or no immunosuppressive treatment. Two or six weeks after transplantation, there was good survival of xenografts in both the methylprednisolone- and cyclosporin A-treated rats. In contrast, the xenografts in untreated control rats were all rejected by six weeks. There was no marked difference in the degree of expression of MHC class I and II antigens and the accumulation of activated astrocytes and microglial cells/macrophages between the three groups. However, both methylprednisolone and cyclosporin A reduced infiltration of T lymphocytes to the transplantation sites. The expression of pro-inflammatory cytokines (interferon-γ, tumor necrosis factor-α, interleukin-6) in and around the grafts was lower in the methylprednisolone- and cyclosporin A-treated groups than in untreated control rats. Although high-dose methylprednisolone caused significant body wt. loss, this treatment can prevent rejection of intrastriatal grafts of xenogeneic embryonic neural tissue in the adult.

Answer 5:

Bibliographic Information

Phenotypic modification of human glioma and non-small-cell lung carcinoma by glucocorticoids and other agents. McLean, John S.; Frame, Margaret C.; Freshney, R. Ian; Vaughan, Peter F. T.; Mackie, Alison E.; Singer, Iain. Dep. Med. Oncol.,

Univ. Glasgow, Glasgow, UK. Anticancer Research (1986), 6(5), 1101-6. CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 106:113720 AN 1987:113720 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Glucocorticoids were cytostatic for human glioma growth at a high cell d. in cell culture. The effect was not cytotoxic, appeared to involve a modification of the cell surface, and was detected with methylprednisolone [83-43-2], dexamethasone [50-02-2] and betamethasone [378-44-9]. Glucocorticoids also reduced malignancy-assocd. properties (plasminogen activator [105913-11-9] and endothelial mitogenesis) and enhanced differentiation (glutaminyl synthetase [9023-70-5] activity and high affinity GABA [56-12-2] uptake). Cytostasis was also seen at high cell densities in non-small-cell lung carcinoma with a concomitant redn. in plasminogen activator activity and endothelial mitogenesis. Preliminary data on surfactant prodn. in A549 cells suggests that the repression of malignancy-assocd. properties is accompanied by an increase in cell differentiation. Treatment of the WIL adenocarcinoma grown as a xenograft in nude mice caused total cessation of growth and massive central necrosis in the tumor.

Answer 6:

Bibliographic Information

Aplidin synergizes with cytosine arabinoside: functional relevance of mitochondria in Aplidin-induced cytotoxicity. Humeniuk R; Menon L G; Mishra P J; Saydam G; Longo-Sorbello G S A; Elisseyeff Y; Lewis L D; Aracil M; Jimeno J; Bertino J R; Banerjee D Department of Medicine and Pharmacology, The Cancer Institute of New Jersey, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, New Brunswick, NJ 08903, USA Leukemia : official journal of the Leukemia Society of America, Leukemia Research Fund, U.K (2007), 21(12), 2399-405. Journal code: 8704895. E-ISSN:1476-5551. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 17713546 AN 2007697981 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Aplidin (plitidepsin) is a novel marine-derived antitumor agent presently undergoing phase II clinical trials in hematological malignancies and solid tumors. Lack of bone marrow toxicity has encouraged further development of this drug for treatment of leukemia and lymphoma. Multiple signaling pathways have been shown to be involved in Aplidin-induced apoptosis and cell cycle arrest in G1 and G2 phase. However, the exact mechanism(s) of Aplidin action remains to be elucidated. Here we demonstrate that mitochondria-associated or -localized processes are the potential cellular targets of Aplidin. Whole genome gene-expression profiling (GEP) revealed that fatty acid metabolism, sterol biosynthesis and energy metabolism, including the tricarboxylic acid cycle and ATP synthesis are affected by Aplidin treatment. Moreover, mutant MOLT-4, human leukemia cells lacking functional mitochondria, were found to be resistant to Aplidin. Cytosine arabinoside (araC), which also generates oxidative stress but does not affect the ATP pool, showed synergism with Aplidin in our leukemia and lymphoma models in vitro and in vivo. These studies provide new insights into the mechanism of action of Aplidin. The efficacy of the combination of Aplidin and araC is currently being evaluated in clinical phase I/II program for the treatment of patients with relapsed leukemia and high-grade lymphoma.

Answer 7:

Bibliographic Information

Immune parameters relevant to neural xenograft survival in the primate brain. Cicchetti F; Fodor W; Deacon T W; van Horne C; Rollins S; Burton W; Costantini L C; Isacson O Neuroregeneration Laboratories, Harvard Medical School/McLean Hospital, Belmont, MA, USA. fcicchetti@mclean.harvard.edu Xenotransplantation (2003), 10(1), 41-9. Journal code: 9438793. ISSN:0908-665X. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 12535224 AN 2003029187 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

The lack of supply and access to human tissue has prompted the development of xenotransplantation as a potential clinical modality for neural cell transplantation. The goal of the present study was to achieve a better understanding of the immune factors involved in neural xenograft rejection in primates. Initially, we quantified complement mediated cell lysis of porcine fetal neurons by primate serum and demonstrated that anti-C5 antibody treatment inhibited cell death. We then developed an immunosuppression protocol that included in vivo anti-C5 monoclonal antibody treatment, triple drug therapy (cyclosporine, methylprednisolone, azathioprine) and donor tissue derived from CD59 or H-transferase transgenic pigs and applied it to pig-to-primate neural cell transplant models. Pre-formed alphaGal, induced alphaGal and primate anti-mouse antibody (PAMA) titers were monitored to assess the immune response. Four primates were transplanted. The three CD59 neural cell recipients showed an induced anti-alphaGal response, whereas the H-transferase neural cell recipient exhibited consistently low anti-alphaGal titers. Two of these recipients contained surviving grafts as detected by immunohistochemistry using selected neural markers. Graft survival correlated with high dose cyclosporine treatment, complete complement blockade and the absence of an induced PAMA response to the murine anti-C5 monoclonal antibodies.

Answer 8:

Bibliographic Information

Visualization of antigen-specific T cell activation in vivo in response to intracerebral administration of a xenopeptide. Ni H T; Merica R R; Spellman S R; Wang J M; Low W C Department of Neurosurgery, University of Minnesota, Minneapolis, Minnesota 55455, USA Experimental neurology (2000), 164(2), 362-70. Journal code: 0370712. ISSN:0014-4886. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 10915575 AN 2000412042 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Allogeneic or xenogenic tissues exhibit prolonged survival when grafted into the brain parenchyma in comparison to grafting into peripheral sites. The brain, therefore, has long been considered an immunologically privileged site. However, the immunological privilege of the brain is not absolute, and it cannot shield neural xenografts from rejection. In our laboratory, we are interested in determining how to prevent neural xenograft rejection. To do so, we need to first understand how the immune system responds to CNS antigens leading to graft rejection. In order to monitor immune system responses to CNS antigens an adoptive transfer system was used to directly track CNS antigen-specific CD4(+) T cell responses in vivo. This would then allow us to monitor changes in the number, activation state, and anatomic distribution of antigen-specific cells. We have found that, after intracerebral injection of xeno peptide antigens with adjuvant, antigen-specific cells accumulated in the cervical lymph node, proliferated there for several days, and then disappeared slowly from the nodes. Interestingly, peptide antigens given intracerebrally also stimulated a strong antigen-specific CD4(+) T cell response. Moreover, cells remaining in the lymph node 8 days after antigen stimulation produce IL-2 with secondary antigenic challenge. Previous studies have shown that the administration of antigens without adjuvant in a monomeric form via either the intraperitoneal or intravenous route has failed to induce cell-mediated immunity and resulted in antigen-specific T cell unresponsiveness. Our findings demonstrate that antigen delivered intracerebrally can activate immune responses in a manner different than antigen delivered to peripheral sites outside of the CNS. Copyright 2000 Academic Press.

Answer 9:

Bibliographic Information

In vitro and in vivo anti-leukemic efficacy of cyclic AMP modulating agents against human leukemic B-cell precursors. Myers D E; Chandan-Langlie M; Chelstrom L M; Uckun F M University of Minnesota Biotherapy Program, Roseville 55113, USA Leukemia & lymphoma (1996), 22(3-4), 259-64. Journal code: 9007422.

ISSN:1042-8194. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 8819074 AN 96416168 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

We show that the adenylate cyclase activating diterpine, forskolin, the phosphodiesterase inhibitor, aminophylline, and the permeant cAMP analog dibutyryl cAMP inhibit the in vitro clonogenic growth of leukemic B-cell precursors. We also used a SCID mouse xenograft model of refractory human B-cell precursor leukemia to evaluate the anti-leukemic effect of aminophylline in vivo. Treatment with aminophylline (6 mg/kg bolus followed by 0.1-0.5 mg/kg/hour x 7 days) significantly prolonged the event-free survival of SCID mice (median survival of control mice, 39 days, N = 79; median survival of aminophylline-treated mice, 60 days, N = 10; P < 0.0001 by log-rank test) and it was more effective than treatment with vincristine (median survival = 51 days, N = 5) or L asparaginase (median survival = 44 days, N = 5). However, aminophylline was not as effective as methylprednisolone (median survival: 103 days, N = 5). These results indicate that cAMP modulating agents may be useful in treatment of refractory human B-cell precursor leukemia.

Answer 10:

Bibliographic Information

Methods of immunosuppression for study of growth and lung colony formation by human tumor cells in mice. Kovnat A; Khoo K; Selby P; Tannock I Cancer research (1986), 46(4 Pt 1), 1617-22. Journal code: 2984705R. ISSN:0008-5472. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T); (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.) written in English. PubMed ID 3512076 AN 86133218 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Mice that are immune-suppressed by thymectomy and by sequential treatment with 1-beta-D-arabinofuranosylcytosine and whole body irradiation may be used as hosts for generation of human tumor xenografts. We have studied the effect of various additional methods of immune suppression on the formation of tumors after i.m. injection and on the formation of lung colonies after i.v. injection with the human MGH-U1 bladder cancer cell line. Success of transplantation was improved by treatment of immune-suppressed animals with either heterologous antilymphocyte serum or a monoclonal anti-Thy-1.2 antibody. Success of lung colony formation was also improved by antilymphocyte serum but not by monoclonal anti-Thy-1.2 antibody. Admixture of heavily irradiated cells (10(6)) to the viable inoculum of tumor cells in addition to antilymphocyte serum treatment improved the success of i.m. transplantation but not that of lung colony formation. Treatment with corticosteroids or treatment with carrageenan to suppress macrophage activity added toxicity and did not improve the success of xenografting. Immune suppression decreased the natural killer cell activity of normal mice and treatment with antiinterferon to further suppress natural killer cells may also enhance xenograft formation. Administration of cyclosporin A to normal mice allowed the growth of a single xenograft but was not a useful method for immunosuppression. The success of xenografting into immune-deprived mice was superior to that for two strains of nude mice maintained in our laboratory, and i.v. injection of tumor cells did not lead to lung colonies in these nude mice. Immune-deprived mice are a useful alternative to nude mice for the study of xenografts derived from human tumor cell lines and may allow the study of experimental lung metastases.